

CARDIAC ABNORMALITIES IN PATIENTS WITH CIRRHOSIS**NANDYALA VENKATESHWARLU^{a1}, P. GANDIAH^b, G. INDIRA^c, P. SIVARAJAPPA^d
AND K. K. PRABHAKAR^e**^{abcde}Department of General Medicine, SVS Medical College, Mahabubnagar, A.P., India**ABSTRACT**

Cardiac abnormalities have been studied by many researchers. Advanced liver cirrhosis is associated with an increase in blood volume, a reduction in systemic vascular resistance, and an increase in cardiac output. How this hyperkinetic circulation affects cardiac function and structure has been incompletely described. Patients with cirrhosis, who have overt cardiac dysfunction, may or may not manifest clinically with symptoms or signs. All patients with cirrhosis of liver should be screened for structural and functional cardiac abnormalities, irrespective of age, sex or cause of cirrhosis. Increased levels of serum bilirubin, INR and serum creatinine are associated with higher degree of cardiac abnormalities. Increase in MELD's criteria score is directly proportional to the increase in risk of cardiac abnormalities. Patients who are on transplant recipient list should be screened for latent cardiac abnormalities, so as to prevent death due to arrhythmias. Patients with structural or functional cardiac abnormalities before transplant should be closely monitored for worsening of cardiac function after the transplantation of liver. Cirrhosis was seen predominantly in older age group with 94% of patients >40 yrs, of which 66 % were in between 41 and 60 yrs of age. Cirrhosis of liver was predominantly seen in males i.e. 31 cases (62%) compared to females 19 cases (38 %). The commonest cause of cirrhosis was chronic alcoholism, followed by viral hepatitis. ECG changes seen in 44 % of the cases were long QTc interval. Functional cardiac dysfunction (96%) was higher compared to structural cardiac abnormality (66%).

KEYWORDS : Cirrhosis of Liver, Cardiac abnormalities, ECHO, Severity of Cirrhosis

Cirrhosis is a common hepatological disorder seen in clinical practice. Cirrhosis is a pathologically defined entity that is associated with a spectrum of characteristic clinical manifestations. Cardiac abnormalities have been studied by many researchers, of which Kowalski and Abelmann, 1953 were the first to report that patients with cirrhosis had abnormal cardiovascular function and a prolonged QTc interval. Advanced liver cirrhosis is associated with an increase in blood volume, a reduction in systemic vascular resistance, and an increase in cardiac output. How this hyperkinetic circulation affects cardiac function and structure has been incompletely described. Evidence has been produced that left ventricular systolic function is usually normal at rest in cirrhotic patients, scanty information is available on whether this applies to diastolic function and cardiac structure as well. (Puddu and Bourassa, 1986).

This is of pathophysiological relevance because in other diseases diastolic function has proved to be an early marker of cardiac structural abnormality that in advanced cirrhosis may be favoured by the influence that stimulation of the renin-angiotensin-aldosterone and the sympathetic nervous systems exerts on tissue growth.

Hence, this study will evaluate the clinical aspects of cirrhosis, its effect on cardiac functions and structure by

means of echocardiogram.

MATERIALS AND METHODS

Total 50 patients of age group >18 years, diagnosed as Cirrhosis of liver were studied thoroughly with regards to both history and clinical examination. 50 normal persons (age and sex matched) served as normal. A thorough clinical and biochemical and ultrasound scan undertaken. All the 100 patients underwent a thorough 2-dimensional echocardiography (2D ECHO).

Statistical Software

The Statistical software namely SAS 9.2, SPSS 15.0, Stata 10.1, MedCalc 9.0.1, Systat 12.0 and R environment ver.2.11.1 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc.

RESULTS AND DISCUSSION

Age distribution ranged widely with youngest patient being 38 years and oldest patient of 78 years. Cirrhosis and SBP was seen predominantly in older age group with 94% of patients >40 yrs, of which 66 % were in between 41 and 60 yrs of age in table 1. Mean age was 56 years.

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Table 1: Age Distribution

Age in years	Number of patients	%
18 - 40	3	6.0
41 - 60	33	66.0
61 - 80	14	28.0
Total	50	100.0

Mean ± SD: 55.64±10.02

Table 2: Gender Distribution

Gender	Number of patients	%
Male	31	62.0
Female	19	38.0
Total	50	100.0

Cirrhosis of liver was predominantly seen in males i.e 31 cases (62%) compared to females 19 cases (38 %). in table 2.

Etiology of Cirrhosis

The most predominant cause of cirrhosis was chronic alcoholism; most of them gave h/o daily consumption of alcohol for over at least 20 yrs. All the alcoholics were abstinent for at least a year or more before the study. Of the other 28%, 18% were detected to have chronic hepatitis with most of them on irregular or no treatment for the same. Etiology of the rest 10 % of the cases couldn't be identified in figure,1.

Table 3: ECG Changes

ECG changes	Number of patients (n=50)	%
Yes	23	46.0
No	27	54.0

Of the 23 cases with ECG changes 20 had long QTc intervals, and the other three with non significant ST elevation changes.(Table,3)

QTc i.e. heart rate corrected QT interval was calculated using Bazett(1920) formula.

The LAD and LVED were above normal limits in all patients of the study group, with the mean value for LAD being 39.96±1.34mm and that of LVED being 40.38±1.03 mm, which directly reflects on the LV mass in table 4.

Table, 5 shows that LV mass in 66 % of the patients were more than normal limits (male >170gms and female >160gms), with a mean value of 169.30±26.04gms.

The e/a ratio in 96 % of the patients are <1.3 for male and <1.2 for female with 98% of the group having an E/A ratio of less than or equal to 1. Mean value of E/A ratio was 0.89±0.16.

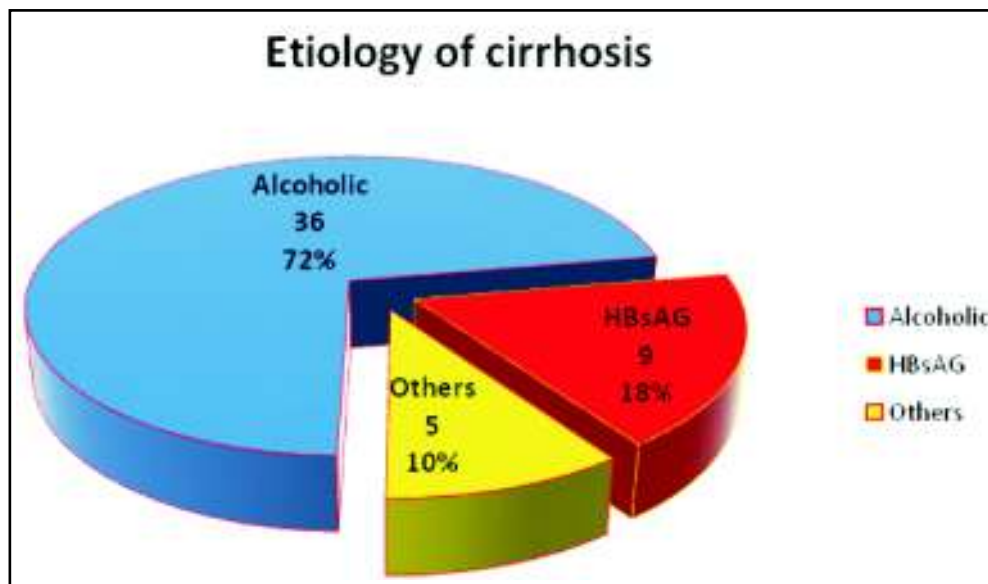


Figure 1: Etiology of Cirrhosis

Table 4: ECHO Cardiography

Echo-Cardiac parameters	Criteria(mm)	Number of patients (n=50)	%	Mean ± SD(mm)
LAD mm	25-35 (normal)	0	0.0	39.96±1.34
	>35	50	100.0	
LVED mm	28-32(normal)	0	0	40.38±1.03
	>32	50	100.0	

Table 5: ECHO Parameters

LV mass	Male <170; female <160	17	34.0	169.30±26.04
	Male >170 Female >160	33	66.0	
Ejection fraction	Male :55-75 Female: 55-80	50	100.0	64.53±0.97
	Male : >75 Female:>80	0	0.0	
E/A ratio	Male <1.3; Female <1.2	48	96.0	0.89±0.16
	Male >1.3; Female >1.2	2	4.0	

Out of the 33 patients that had the abnormal LV mass 57.6% were of the 41 to 60 age group closely followed by 39.4% of the group in 61 to 80 yrs age group in table 6.

Table 6 :Significance of Age With LV Mass

Age in years	LV MASS			
	Normal : Male < 170; female <160 (n=17)		Abnormal Male >170; Female >160 (n=33)	
	No	%	No	%
18 - 40	2	11.8	1	3.0
41 - 60	14	82.4	19	57.6
61 - 80	1	5.9	13	39.4

Of the no. of cases whose E/A ratio is below normal limits (48) the lowest mean was in the 61 to 80 yrs category, while the maximum no. of cases with mean E/A ratio below the normal limit was in the 41 to 60 yrs (32) in figure 2.

LV mass of patients did not show any significant statistical correlation with alcohol consumption as 70.6% of the patients with normal LV mass consumed alcohol and 72.7% of those who had abnormal LV mass had h/o alcohol consumption in table 7.

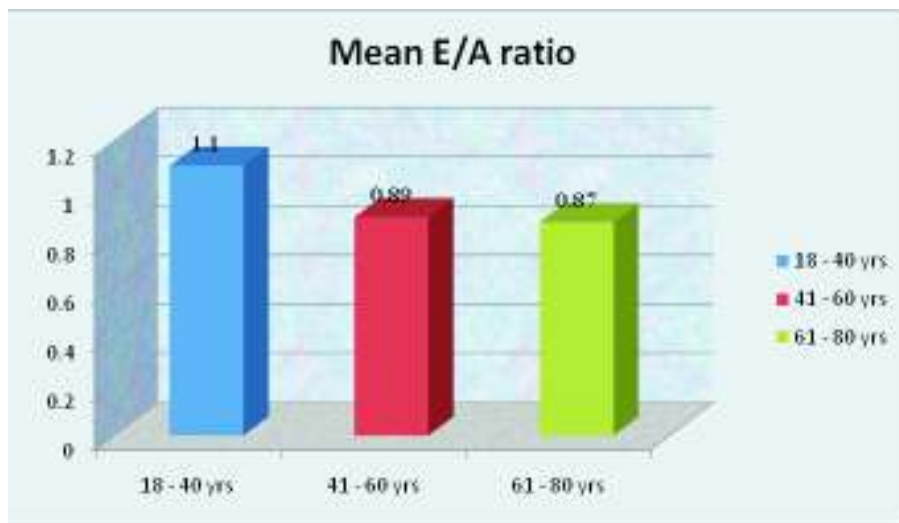


Figure 2 : Significance of Age With E/A ratio

Table 7: Alcohol Consumption and LV Mass

Alcohol consumption	LV MASS			
	Normal : Male <170; female <160 (n=17)		Abnormal Male >170; Female>160 (n=33)	
	No	%	No	%
No	5	29.4	9	27.3
Yes	12	70.6	24	72.7

The reasoning for the same could be because of the lower percentage of patients who did not consume alcohol in the study group.

BMI vs LV mass

BMI showed no significant correlation with LV mass as all the groups in both normal and abnormal LV mass had almost similar distribution in table 8.

Table 8 :BMI and LV Mass

BMI (kg/m ²)	LV MASS			
	Normal : Male <170; Female <160 (n=17)		Abnormal Male >170; Female>160 (n=33)	
	No	%	No	%
<18.5	0	0.0	5	15.2
18.5-25.0	7	41.2	10	30.3
25.0-30.0	6	35.3	10	30.3
>30.0	4	23.5	8	24.2

BMI showed no significant correlation with E/A ratio as the the mean E/A ratio remained similar throughout the divisions of BMI in table 9.

Table 9: BMI and E/A Ratio

BMI (kg/m ²)	Mean E/A ratio
<18.5	0.92±0.15
18.5 - 25.0	0.85±0.17
25.0 - 30.0	0.93±0.19
>30.0	0.91±0.10

Child Pugh Score And Meld's Criteria

All patients were in CLASS C child Pugh's criteria. All patients in the study had a MELD'S criteria score of more than 40, which showed significant correlation with cardiac structural and functional abnormalities in figure 3.

Number of Patients in Different Studies

In our study the number of patients who had cirrhosis was 50, as compared to Florence Wong et al study which had 32 patients with cirrhosis and 48 as controls .

Age and Sex in Different Studies

Mean age the study group was 56 ± 10 yrs as compared to Wong et al. ,(1999) study whose was 52 ± 4 yrs. This is probably due to the larger study group than the latter study.

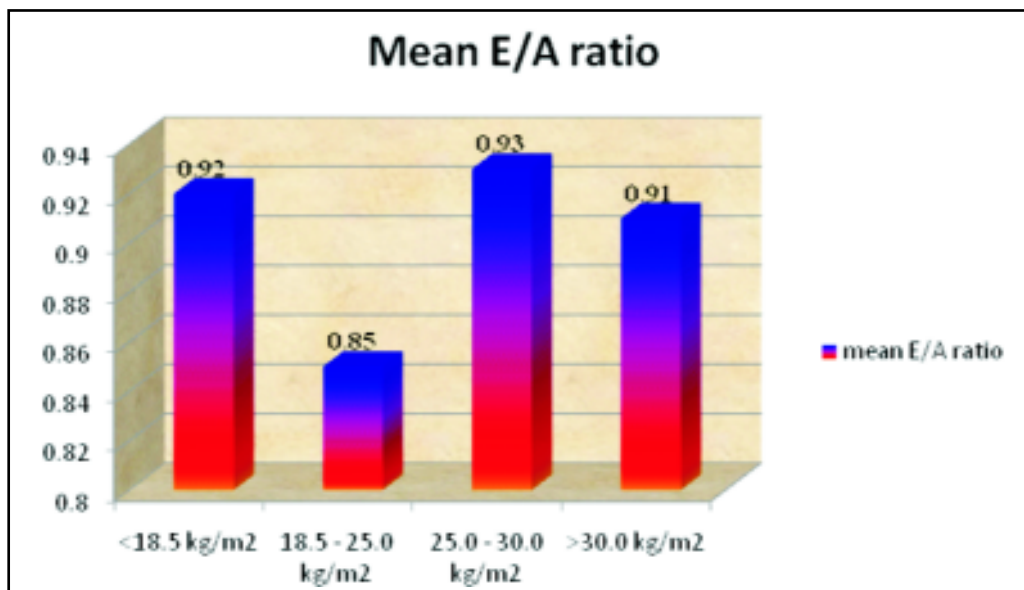


Figure 3 :BMI and E/A Ratio

Table 10 : Numer of Patients With Cirrhosis in Different Age and Sex

Parameters	Present Study	Wong.F. et al.,(1999)	P.Liu et al.,(2001)	Pozzi.M. et al.,(1997)
No. of patients with cirrhosis	50	35	39	27
Male	31	32	37	21
Female	19	3	3	6

The patients were predominantly males i.e., 31 cases male (62 %) to 19 cases female (38 %) while the male to female ratio in three studies of Wong et al.,(1999),Liu et al.,(2001) and Pozzi et al.,(1997) were 32 male cases to 3 cases female, 37 cases male to 2 cases female and 21 cases male to 6 female respectively. This could be probably explained by the larger no. of males with history of consumption of alcohol for prolonged periods of time in table 10.

In the present study, 33 patients that had the abnormal LV mass, 57.6% were of the 41 to 60 age group followed by, 39.4 % of the group in 61 to 80 yrs age group, which showed a significant correlation of this age group(41 60) to have more chances of having overt cardiac abnormalities.

Only 44% of the patients (22 cases) had complaints of chest pain of which most were retrosternal, burning type of pain and had previous episodes of the same for which they were treated as acute gastritis. Even so, 82% (18 cases) of this group had abnormal LV mass findings indicating that, many patients with cirrhosis of liver may not present with any cardiac signs or symptoms and should be subjected to careful cardiac evaluation and 2D ECHO. Clinically all the patients moderate to severe ascites, of which 40% had tense ascites and in the rest shifting dullness could be elicited. Icterus was seen in 74 % of the cases. Signs of liver cell failure were noticed only in 12 % of the cases of which correlation with structural or functional cardiac function was not significant. Hence highlighting the importance of cardiac screening in patients who present with minimal or no signs of liver cell failure.

The most predominant cause of cirrhosis of liver in this study was alcoholism with 72 % of the study

Table 11: Etiology of Cirrhosis (Wong et al.,1999)

Etiology	Present Study (no.)	Wong et al., (1999)
Alcohol	36	24
Hepatitis	9	6
Other	5	5

population being alcoholics for more than 15 yrs. The rest 28 % of the population consisted of chronic hepatitis patients (18%) and other unknown causes of cirrhosis in comparison to the Wong.et al.,(1999) study which had 68.5 % alcoholics and 17.1 % cases of chronic hepatitis in table 11.

The cardiac abnormalities in the group did not show any significant correlation to any particular etiology. This impresses upon the importance of latent cardiac abnormalities in cirrhosis patients irrespective of the cause for which they should be screened.

This observation is also in accordance with the Pozzi et al.,(1997) study which found no difference in the cardiac abnormalities caused by alcoholic cirrhosis and those by post viral cirrhosis, along with stating that the diastolic dysfunction in the subjects were unlikely to be caused by the toxic effects of ethanol on the heart.

Liver Function Tests in Cirrhosis

Of the liver function tests, importance was given to serum bilirubin, serum albumin.

Serum bilirubin was raised in all patients with a mean value of 6.36mg/dl, which showed significant correlation to the severity of cardiac abnormalities. Serum albumin level was low in most of the patients with the mean value being 2.03mg/dl. The hypoalbumunemia may be one

of the causes of cardiac diastolic dysfunction due to increased preload to the heart by fluid retention in the body as stated in the study by Honker et al.,1999.

Hyponatremia and Cardiac Abnormalities in Cirrhosis

About 48 % of the study population had mild to moderate hyponatremia (<135 mEq/L) with a mean of 135.86 ± 3.21 mEq/L similar to that of Pozzi et al.,1997 study which had 134.2 mEq/L as a mean value. Even though the present study could not place a relevant significance between hyponatremia and the diastolic dysfunction in cirrhotics, The Pozzi et al.,1997 study and the Wong et al.,1999 study points out a significant correlation between hyponatremia and diastolic dysfunction, stating the reason for hyponatremia to be that of initially the nitric oxide, which is involved in the myocardial contractile dysfunction. An inadequate cardiac response for the extent of the decrease in the afterload may aggravate the sodium handling abnormality that is already present in cirrhosis. In turn, sodium retention may aggravate myocardial dysfunction, hastening the development of refractory ascites, hence giving rise to a 'vicious cycle'.

Child Pugh's Score and Meld's Criteria to Predict Severity of Cardiac Abnormality

All the patients in the study group had Child Pugh's classification CLASS C . While the child Pugh's score correlation with cardiac structural and functional abnormalities did not reach any level of significance, the MELD score showed increasing severity of cardiac abnormalities as the score rose above 40. This probably due to the fact that MELD criteria score being calculated on the serum bilirubin, INR and serum creatinine levels, rise in these factors directly causes deterioration in cardiac functionality.

Ecg Changes and Cardiac Abnormalities in Cirrhosis

In the study population 46 % (23 cases) had ECG changes, of which 20 cases had long QTc intervals. These cases showed a significant correlation with cardiac deformities in accordance with the Bernadi et al.,1998.. Long QTc is associated with sudden death due to arrhythmias 10. Hence careful cardiac evaluation of those

Table 12 : Echocardiographic Parameters In Cirrhosis

Parameters	Present study	Wong et al.,1999	Pozzi et al.,1997
LAD(mm)	39.96±1.34	40±1	41±1
LVED(mm)	40.38±1.03	41±1	41±1
LVEF (%)	64.53±0.97	62.7±3.6	63.4±2.8

with long QTc intervals is mandatory as they are in the high risk for cardiac abnormalities which may not be picked up clinically.

Echocardiographic Parameters in Cirrhosis

The LAD and LVED were above normal limits in all patients of the study group, with the mean value for LAD being 39.96±1.34 mm and that of LVED being 40.38±1.03 mm. which directly reflects on the LV mass as is shown in the studies my Wong et al.,1999 and Pozzi et al.,1997(Table,12).

LVEF was normal in all the patients of the study group, with mean value of 64.53±0.97 %, similar to results in same above mentioned studies. This paradoxical normal EF value in the face of diastolic dysfunction could probably be because of normal pre and afterload of the cirrhotic heart as explained by Muller et al.,2009.

LV mass was significantly raised in 66 % of the study population with a mean value of 169.30±26.04 gms, which is accordance with the Wong et al.,1999 study along with E/A ratio being ≤ 1 in 96 % of the population in table 13.

The major cardiac structural abnormality of the myocardium in such patients was myocardial hypertrophy. One possible explanation for this would be myocardial adaptation to a chronically elevated blood volume. Alternatively, ventricular hypertrophy or remodeling could be related to the trophic effects of activated neurohormonal systems such as noradrenalin, or angiotensin II with or without the synergistic effects of endothelin-1(Yamazaki et al.,1995 and1996).

Table 13 : LV Mass and E/A Ratio Mean

Parameters	Present study	Wong et al., 1999
LV mass mean (gms)	169.30±26.04	171.4±20.04
E/A ratio mean	0.89±0.16	0.9±0.1

CONCLUSIONS

Patients with cirrhosis, who have overt cardiac dysfunction, may or may not manifest clinically with symptoms or signs. All patients with cirrhosis of liver should be screened for structural and functional cardiac abnormalities, irrespective of age, sex or cause of cirrhosis. Increased levels of serum bilirubin, INR and serum creatinine are associated with higher degree of cardiac abnormalities. Increase in MELD's criteria score is directly proportional to the increase in risk of cardiac abnormalities. Patients with structural or functional cardiac abnormalities before transplant should be closely monitored for worsening of cardiac function after the transplantation of liver. ECG changes seen in 44 % of the cases were long QTc interval. Functional cardiac dysfunction (96%) was higher compared to structural cardiac abnormality (66%)

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